09/485267

PATENT COOPERATION TREATY

PCT

REC'D 03 DEC 1999

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
28.66856/004		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB98/02378	07/08/1998	08/08/1997
International Patent Classification (IPC) or national classification and IPC A61K31/27		
Applicant SHIRE INTERNATIONAL LICENSING BV et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
02/03/1999	01.12.99
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Heller, D Telephone No. +49 89 2399 8746

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB98/02378

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-11 as originally filed

Claims, No.:

1-7 as received on 07/10/1999 with letter of 06/10/1999

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☒ the claims, Nos.: 8-17
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-7.

because:

☒ the said international application, or the said claims Nos. 1-7 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-7
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-7
Industrial applicability (IA)	Yes:	Claims	see section III and V
	No:	Claims	

2. Citations and explanations

see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

Section I:

Amendments

The amended claims are allowable under Article 34 (2) b) PCT.

Section III:

Claims 1 to 7 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Section V:

Prior art

Reference is made to the following documents:

D5 (WO92/20328) describes the use of cholinesterase inhibitors, such as galantamine, for the preparation of a pharmaceutical composition for counteracting the sedative or hypnotic or respiratory depressive effects of benzodiazepines (claim 1) given for the treatment of diseases as i.e. hyperactivity of children (claim 27; page 4, line 27).

D6 (US-A-4 550 113) relates to a compound and composition which stimulates neuro-muscular transmission of smooth muscles and causes excitation in the peripheral and central nervous systems which is useful in the treatment of various injuries of the peripheral nervous system with motor disturbances (neuritides, polyneuritides, polyradiculoneuritides), for the treatment of post-effects of the previously incurred vascular injuries of the brain; myasthenia or other neuro-muscular diseases which are inherited; for stimulation of delivery in birth, for the treatment of patients with atony and akinesia of the gastro-intestinal tract and the like.

D7 (Neurology, 1997, 48, page A397) discloses the use of tacrine for the treatment of attention deficit disorder (ADD).

D14 (WO95/29909) relates to a pharmaceutical composition for the treatment of several mental disorders, including attention deficit disorders, comprising an acetylcholine release enhancing amount of a compound and an acetylcholinesterase inhibitor (claims 45 and 46).

D15 (EP-A-0 229 391) compares the acetylcholinesterase inhibitory activity of new compounds with that of physostigmine (page 49, example 1) for the treatment of disturbance of attention (page 15, line 11).

D16 (EP-A-0 441 534) relates to novel derivatives of 1,2,3,4-tetrahydro-9-acridinamine useful as pharmaceutical agents, to pharmaceutical compositions which include these compounds and a pharmaceutically acceptable carrier, and to pharmaceutical methods of treatment, e.g. attention deficit disorders.

D17 (EP-A-0 607 864) compares the acetylcholinesterase inhibitory activity of new compounds with that of physostigmine (page 71, lines 40 to 45) for the treatment of hyperkinesia (page 117, table 76).

Novelty

The subject-matter of claims 1 to 7 is new in the sense of Article 33 (2) PCT.

Galantamine can be given as cholinesterase inhibitor in combination with benzodiazepines (page 5, §1). The benzodiazepines seem to be responsible for the therapeutic effects in the treatment of e.g. hyperactivity of children and galantamine is given to alleviate the undesirable side effects of the benzodiazepines. As there is no disclosure that galantamine has any effects itself in the above-mentioned therapy, present claims 1 to 7 are novel over D5.
D5 is authored by the same inventor as in the present invention.

D6 does not anticipate novelty, because it is silent to the use of galantamine or its derivatives. The same applies for D7 and D14 to D17.

Inventive step

The subject-matter of claims 1 to 7 does not involve an inventive step in the sense of Article 33 (3) PCT.

D5 which is the closest prior art differs from the present invention only in that the benzodiazepines seem to be responsible for the therapeutic effects in the treatment of e.g. hyperactivity of children and galantamine is given to alleviate the undesirable side effects of the benzodiazepines. There is no disclosure that galantamine has any effects itself in the above-mentioned therapy.

The problem to be solved can be described as how to provide further medicaments for the treatment of attention deficit disorders.

As it is well-known from the prior art documents (D7, D14 to D17), that cholinesterase inhibitors can be given to treat attention deficit disorders and as galantamine is a cholinesterase inhibitor, the person skilled in the art would administer galantamine to patients suffering from attention deficit disorders.
Therefore, claims 1 to 7 are not inventive according to Article 33 (3) PCT.

Other objections

For the assessment of the present claims 1 to 7 on the question whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Section VI:

The applicant is informed that no check has been made as to whether priority has been validly claimed. Therefore, documents D1 and D2 (WO98/39000 and WO97/46527), which have been disregarded in writing the present report, could become relevant for the assessment of novelty once the present application enters the regional phase (Rule 64 (1) b PCT).